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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,623	06/20/2003	Uri H. Saragovi	62950-010310	7195

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 05/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,623	SARAGOVI ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-29 and 31-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The Election filed on March 17, 2005 in response to the Restriction Requirement of November 17, 2004 has been entered. Applicants election without traverse of Group III, claim 30, as specifically drawn to a method of by-passing resistance of tumor cells by p-glycoprotein pump (PGP) is acknowledged. Applicants further elected from claim 1 or 4 a chemotherapeutic agent as the ONE therapeutic agent.

The restriction requirement is therefore deemed to be proper and is made FINAL.

Claims 1-34 are currently pending.

Claims 1-29 and 31-34 are withdrawn from consideration as being drawn to non-elected inventions.

Claim 30 is currently under consideration.

Specification

The disclosure is objected to because of the following informalities:

The specification on page 1 should be amended to reflect the priority status of the present application, for example: The present application is a continuation of PCT/CA01/01854 filed on 12/21/2001 which claims priority to Provisional Application Serial No: 60/256,987 filed on 12/21/2000.

The specification on page 16, line 32 recites "Binding pr files of th conjugated antibody s". It appears that the specification should read "Binding profiles of the conjugated antibodies".

Appropriate correction is required.

Claim Objections

Claim 30 is objected to because of the following informalities: Claim 30 recites "... administering the compound of claim 1 to a patient ...." However, claim 1 is a non-elected invention. Appropriate correction is required.

(Note: For examination purposes the compound of claim 1 will be interpreted as a compound of the formula: W-Z-X wherein, X is a chemotherapeutic agent, Z is a breakable linker which links W and X together, and W is a molecule which is adapted to selectively bind said target cell directly or indirectly.)

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "by-passing resistance" in Claim 30 is a relative phrase, which renders the claim indefinite. The phrase "by-passing resistance" is not defined by the claim and the disclosure does not provide a limited definition for ascertaining the requisite degree for the terminology sought in the claims and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention and would not be able to determine the metes and bounds of the claims. In the instant case, it cannot be determined how the compound is bypassing resistance of tumor cells by p-glycoprotein pump (PGP). For example, the claim can be interpreted as by-passing resistance of tumor cells by using a p-glycoprotein pump (PGP) or by-passing resistance of tumor cells mediated by p-glycoprotein pump (PGP). In addition, it cannot be determined whether the tumor cells are resistant or if they are "sensitive". Moreover, it cannot be determined whether a "patient in need of such treatment" relates to a person in need of a treatment that requires by-passing or is a by-passing treatment.

For examination purposes, the claims will be interpreted as by-passing tumor cell resistance mediated by p-glycoprotein pump.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of compounds of the formula W-Z-X which by-pass tumor resistance mediated by p-glycoprotein, wherein X is a chemotherapeutic agent, Z is a breakable linker and W is an antibody. However, the written description in this case only sets forth on species of a compound of formula W-Z-X which by-pass tumor resistance mediated by p-glycoprotein, wherein X is doxorubicin, Z is a cleavable linker, and W is mAb α-IR3.

The specification teaches (page 4, line 31 to page 5, line 10) that the compounds of the invention include, but are not limited to, compounds represented by the formula W-Z-X, wherein X is a therapeutic agent such as a chemotherapeutic agent or an antiviral agent, Z is a cleavable linker which is breakable by pH modification, reduction or enzymatic hydrolysis and W is a molecule which is adapted to selectively bind the target cell directly or indirectly such as an antibody. Specifically, the specification teaches (page 5, lines 17-22) that chemotherapeutic include not only include taxanes, but also any chemotherapeutic agent such as taxane derivatives, doxorubicin, or daunomycin. In addition, the specification teaches (page 6, lines 11-13) that antibodies of the preferred embodiment include monoclonal antibodies MC192, 5C3 or α-IR3. However, the written description (specification, page 10, lines 24-33 and page 24, line 16 to page 24, line 24) only reasonably conveys one species of a compound of formula W-Z-X, wherein X is doxorubicin, Z is a cleavable linker, and W is mAb α-IR3, in association with bypassing the p-glycoprotein-mediated resistance. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of

cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of conjugates that encompass the genus of compounds of formula W-Z-X that bypass p-glycoprotein-mediated resistance nor does it provide a description of structural features that are common to the compounds of formula W-Z-X. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of one species of compounds which bypass p-glycoprotein mediated resistance is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of compounds, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a compound of formula W-Z-X, wherein X is doxorubicin, Z is a cleavable linker, and W is mAb α-IR3, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Kopecek et al. (U.S. 5,258,453 1993).

(Note: Due to the indefiniteness, supra, of claim 30, the phrase "by-passing resistance" will be interpreted as by-passing tumor cell resistance as a result of p-glycoprotein.)

Kopecek et al. disclose a method of minimizing the amount of cancer cells which are resistant to chemotherapy, comprising administering a compound comprising a anticancer drug and a targeting moiety, such as an antibody, linked via a copolymeric carrier, wherein the polymeric carrier is susceptible to lysosomal hydrolysis (abstract; column 1, lines 51-64; column 3, lines 30-39). The patent further teaches (column 2, line 67 to column 3 line 9) that the marcomoleucle enters the cell via receptor-mediated pinocytosis. Thus, while Kopecek et al. do not characterize the cancer cells being resistant to chemotherapy as a result of p-glycoprotein, the effect recited in the preamble would be an inherent property of the referenced method since resistance to chemotherapy in cancer cells is mainly mediated by overexpression of p-glycoprotein as evidenced by Dietro et al. (Braz. J. Med. Biol. Res. 1999; 32; 925-939). Moreover, Kopeck et al.'s method step meets the active steps recited in the claims. Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Hence, even though the claims are drawn to a mechanism by which the compound treat a patient, the claimed method does not appear to distinguish over the prior art teaching of the same or nearly the same method. The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

The following prior art is provided and made of record (although not relied upon) is considered pertinent to applicant's disclosure:

St'astny et al. (Eur. J. Cancer 1999; 35: 459-466) discloses overcoming p-glycoprotein (PGP)-mediated multidrug resistance by antibody-targeted drugs conjugated to N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer carrier.

Webb et al. (U.S. 6,652,864, filed 1998) disclose compounds for intracellular delivery of therapeutic moieties having the general formula B-L-TM, wherein B may be MAb 5C3 or Mab MC192 (entire document, especially column 9, line 60 to column 10 line 13).

Guillemard et al. (Cancer Research 2001; 61: 694-699) teaches taxane-antibody conjugates afford potent cytotoxicity, enhanced solubility and tumor target specificity. The reference does not teach that the by-passing resistance of tumor cells by p-glycoprotein pump.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
5/6/05